REMARKS

Upon entry of the present amendment claims 1, 7, 12, 13, 18, 20, 22, 23 and 25-27 will be pending for consideration. Claims 2-6, 8, 9, 10, 11, 14-17, 19, 21 and 24 are canceled by the present amendment. Claims 25 - 27 are new. Claims 1 and 22 are independent. Reconsideration of the application is respectfully requested.

Applicants believe the present amendment is responsive to the subsequent Office Action dated October 25, 2010 since the present amendment overcomes any lack of unity and further addresses the rejections from the Office Action dated March 12, 2010. In particular, at least independent claim 22 is original, and, thus, has unity with the previously examined claims.

In addition, present claim 1 retains the technical feature of exciting a sample with two wavelengths of light and detecting an optical property change from the sample (emphasis added). Claim 1 clarifies that the two wavelengths of light include a first wavelength and a second wavelength. Further, Applicants clarified the elements of a first confocal excitation beam having the first wavelength of light and a second confocal excitation beam having the second wavelength of light (emphasis added).

The present amendment merely makes explicit, material that was inherent in the application as originally filed, and is therefore, not new matter. In particular, support for claim 25 can be found in the originally filed specification at least at page 2, lines 15-16. Support for claim 26 can be found in the originally filed specification at least at page 9, lines 8-16. Support for claim 27 can be found in the originally filed specification at least at page 5, lines 6-9.

Applicants further note that a Notification of Transmittal of the International Search Report dated March 17, 2003 for Application No. PCT/PH02/00018 submitted in the Information Disclosure Statement mailed August 24, 2005 was not initialed on Form PTO-1449 included with the Office Action. Applicants respectfully submit that the Notification of Transmittal of the International Search Report dated March 17, 2003 for Application No. PCT/PH02/00018 was included in Form PTO-1449

and a copy thereof was submitted therewith. Therefore, Applicants respectfully request a Form PTO-1449 including Examiner's initials on all references submitted in the Information Disclosure Statement submitted August 24, 2005.

In this amendment, Applicants are canceling claims 2-6, 8, 9, 10, 11, 14-17, 19, 21 and 24. Applicant is not conceding that the subject matter encompassed by claims 2-6, 8, 10, 11, 14-17, 19, 21 and 24 is not patentable. Applicants are canceling claims 2-6, 8, 10, 11, 14-17, 19, 21 and 24 solely to facilitate expeditious prosecution of the remaining claims. Applicant respectfully reserves the right to prosecute claims 2-6, 8, 9, 10, 11, 14-17, 19, 21 and 24, and additional claims, in one or more continuing applications.

Applicants are also amending the claims for one or more of (a) correcting an indefinite recital, (b) ensuring an antecedent basis for terms, (c) improving form, (d) improving grammar, or (e) deleting recitals that do not appear to be necessary for patentability. Amendment is intended not to narrow the scope of any term of any claim. Therefore, the doctrine of equivalents should be available for all of the terms of all claims.

In view of distinguishing elements in independent claim 1, independent claim 22 and dependent claims that depend therefrom, Applicants believe the rejections from the Office Action dated March 12, 2010, discussed in further detail below, are rendered moot.

The Office Action dated March 12, 2010, in section 2, rejected independent claim 1, as well as dependent claims 2 - 4, 7 and 18, under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,667,830 to Iketaki (hereinafter "Iketaki").

Independent claim 1, in part, recites a method for optical excitation of a sample via a two color (two-photon) absorption process including generating the first wavelength of light and the second wavelength of light from "a single light source subjected to a Raman shifter" (emphasis added). The single light source is a laser beam, and the laser beam is adjusted by a laser polarizer and a diaphragm.

In contrast, Iketaki provides linear double resonance excitation microscopy. The method provides a linear double resonance absorption process where an excitation photon ($\lambda 1$ = 532 nm) excites the sample from real energy level 2 to a higher real energy level 3. Second excitation photon ($\lambda 2$ = 563 nm) of Iketaki excites the same sample from a lower energy level 1 to vacated level 2. Excitation beams $\lambda 1$ and $\lambda 2$ of Iketaki are collinear and not angled with respect to each other. Two excitation beams $\lambda 1$ and $\lambda 2$ of Iketaki are non-interacting (uncorrelated). With particular reference to FIG. 26, a mode-locked laser is a pump light that "is subjected to a wavelength conversion with a BBO crystal thereby oscillating 2-nd-harmonics ($\lambda 2$) of …the pump light" (col. 29, lines 34-40). A half mirror is provided by which a portion of the 2nd ($\lambda 2$) harmonics…is extruded and subjected to a wavelength conversion…by a Raman shifter." (Col 29, lines 43-47) (emphasis added).

Iketaki only subjects a portion of the pump light to a Raman shifter. Iketaki specifically provides that a BBO crystal oscillates 2nd harmonics of the pump light thereby creating two wavelengths. In contrast, claim 1 provides for generating a first wavelength of light and a second wavelength of light from a single light source subjected to a Raman shifter. Thus, Iketaki does not disclose claim 1, but instead generates two wavelengths of light through a different method, namely use of a BBO crystal. Further only a portion of the 2nd ($\lambda 2$) harmonics is used as a pump light for a Raman shifter, not the entire laser beam. Claim 1, in part, provides "generating the two excitation wavelengths first wavelength of light and the second wavelength of light from a single light source, subjected to a Raman shifter…wherein the light source is a laser beam." (emphasis added). Claim 1does not parse, divide, or otherwise alter the laser light prior to being subjected to a Raman shifter. Thus Iketaki, generating two wavelengths from a BBO crystal and further subjecting only a portion of the 2nd harmonics to a Raman shifter, does not achieve "a single light source subjected to a Raman shifter" as in claim 1. Therefore, Iketaki does not anticipate claim 1.

Claims 2 - 4 are cancelled rendering rejection under 35 U.S.C. § 102(e) moot. Claims 7 and 18 depend from claim 1. By virtue of this dependence claims 7 and 18 are also allowable over Iketaki. Accordingly, Applicants submit that independent claim 1 and dependent claims therefrom are allowable over Iketaki. Reconsideration and withdrawal of the rejection to claims 1, 7 and 18 are respectfully requested.

The Office Action dated March 12, 2010, in section 4, rejected independent claims 1 and 22, as well as dependent claims 7, 18-21 and 24 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,369,928 to Mandella et al. (hereinafter "Mandella") in view of U.S. Patent No. 6,208,886 to Alfano (hereinafter "Alfano").

Independent claim 1, in part, recites a method including generating the first wavelength of light and the second wavelength of light from a single light source subjected to a Raman shifter (emphasis added).

Mandella provides nonlinear two-color (two-photon) excitation; however, the excitation beam is not from a Raman shifter (emphasis added). Instead, Mandella provides a light source that is split into "first and second beams" by a "half-silvered mirror". (col. 24, lines 26-66) The "first beam is then directed to a frequency doubler" (col. 24, lines 64-66). Further, Mandella provides two fiber-coupled excitation beams $\lambda 1$ and $\lambda 2$ that are confocal in sample space, but the beams are angled with respect to each other (dual illumination axis) using a scanning mirror.

Alfano provides a nonlinear multi-photon absorption process where photons are the same wavelength. In two-photon excitation, $\lambda 1 = \lambda 2$, Alfano provides only one laser beam for illuminating an in vivo biological tissue. The laser beam provided in Alfano is not from a Raman shifter (emphasis added). The method provided by Alfano is for nonlinear multiphoton excitation tomography.

The combination of Mandella and Alfano do not disclose the method and apparatus of independent claim 1. Specifically, neither Mandella nor Alfano disclose or suggest "a single light source subjected to a Raman shifter, wherein the single light source is a laser beam" as recited by claim 1. Further subjecting the single laser in Alfano to the Mandella half-silvered mirror and frequency doubler does not achieve either "generating a first wavelength and a second wavelength of light from a single light source subjected to a Raman shifter" as in claim 1. Thus, the excitation beams in Mandella and Alfano are not "a single light source subjected to a Raman shifter, wherein the single light source is a laser beam" as recited by claim 1. Therefore, claim 1 is allowable over Mandella in view of Alfano.

Claims 19, 21 and 24 are canceled rendering rejection under 35 U.S.C. § 103(a) moot. Claims 7, 18 and 20 depend from claim 1. By virtue of this dependence, claims 7, 18 and 20 are allowable over Mandella in view of Alfano. Accordingly, reconsideration and withdrawal of the rejection as to claims 1, 7, 18 and 20 are respectfully requested.

Independent claim 22 provides, in part, an apparatus for the optical excitation of a sample comprising a light source, an excitable sample, two confocal excitation beams of two different wavelengths, a sample holder, and a mechanism to move the holder in three possible orthogonal directions.

Mandella further provides two fiber-coupled excitation beams $\lambda 1$ and $\lambda 2$ that converge on a sample angled by a scanning mirror. (Abstract). Scanning is achieved by pivoting the illumination beams and their corresponding observation beams.

Alfano further provides a nonlinear multi-photon absorption process for vivo biological tissue where photons are the same wavelength. In two-photon excitation, $\lambda 1 = \lambda 2$. Alfano provides only one focused excitation beam. Further, a mechanism is provided to move the laser relative to the stage in an x, y, z directions (Abstract).

The combination of Mandella and Alfano render one or all of Mandella and Alfano unfit for their intended purposes thus making them improper to combine. As discussed above Mandella provides nonlinear two-color (two-photon) excitation with scanning accomplished by pivoting an illumination beam. Alfano, in contrast, provides for moving a laser relative to the stage in x, y, z directions. Mandella provides a pivoting illumination beam, while Alfano provides a moving platform. If Mandella is modified by Alfano, Mandella is rendered unfit for its intended purpose. The structural setup of Mandella requires a dual illumination axis focused by a single scanning element. If the sample in Mandella were shifted, it would frustrate a focal point of the two illumination beams thereby rendering any scanning of the sample inoperable. Further, if the single wavelength of light used in Alfano were modified by Mandella to provide illumination beams with a $\lambda 1$ and $\lambda 2$ the "light emerging

from an in vivo bio logical tissue" would not comprise "fundamental light, harmonic wave light, and fluorescence" as required for the disclosed detectors. Thus, it is improper to combine Mandella and Alfano.

Further, when analyzed separately, neither Alfano nor Mandella achieve claim 22. In particular, Mandella provides for a scanning a sample by pivoting an illumination beam. Claim 22, in contrast, provides for a mechanism to move the holder (of a sample). Thus, pivoting an illumination beam is not a mechanism to move the holder of a sample as in claim 22. Alfano provides a nonlinear multi-photon absorption process for vivo biological tissue where photons are the same wavelength. In contrast, claim 22 provides two confocal excitation beams of two different wavelengths. Thus, Alfano discloses a photon for vivo biological tissue where photons are the same wavelength and does not achieve claim 22 that provides for two different wavelengths of light. Therefore, neither Alfano nor Mandella, alone or in combination, disclose claim 22.

Dependent claim 24, as mentioned above, is canceled rendering rejection under 35 U.S.C. § 103(a) moot. Accordingly, reconsideration and withdrawal of the rejection to claim 22 are respectfully requested.

The Office Action dated March 12, 2010, in section 5, rejected dependent claims 2-6, 10-15 and 23 under 35 U.S.C. § 103(a) as being unpatentable over Mandella in view of Alfano in further view of Bickel, G.A. et al., *Journal of Chemical Physics* 1987, 86, 1752-1760 (hereinafter "Bickel").

Claims 2-6 and 10-15 are cancelled rendering such rejection moot. However, present independent claim 1, in part, incorporates some distinguishing features of claims 5 and 6. Thus, notwithstanding the cancellation of claims 5 and 6, a discussion is provided to further highlight the distinguishing elements of claim 1. Moreover, a subsequent discussion is also provided to address rejection of dependent claim 23.

In particular, present independent claim 1 incorporates, among other elements, a Raman shifter from canceled claims 5 and 6. In addition, claim 1 recites "collimating an output from the Raman

shifter with a lens, a first dichroic mirror associated with a first beam dump, and a second dichroic mirror associated with a second beam dump."

Mandella, discussed above, provides for nonlinear two-color (two-photon) excitation with two excitation beams derived from a single laser subjected to a half-silvered mirror and a frequency doubler (col. 24, lines 46-50).

Alfano, discussed above, provides a nonlinear multi-photon absorption process for vivo biological tissue where photons are the same wavelength. Further, Alfano discloses a mechanism to move the laser relative to the stage in an x, y, z directions (Abstract). The excitation beam of Alfano is not from a Raman shifter.

Bickel provides nonlinear two-color (two-photon) excitation of a sample. Two excitation beams $\lambda 1$ and $\lambda 2$ of Bickel are collinear and delivered to sample space using a dispersing prism-slit-Fresnel rhomb-focusing lens combination. Beams $\lambda 1$ and $\lambda 2$ of Bickel are produced by the same dye laser pumped Raman shifter. The dye laser is pumped by a 532 nm Nd:YAG laser. Bickel reported two-photon excitation of glyoxal with a Raman shifter, and, also reported two-color (two-photon) excitation of glyoxal with same Raman shifter.

Mandella in view of Alfano, in further view of Bickel, neither disclose nor suggest present independent claim 1. Although Bickel discloses two excitation beams with a Raman shifter, the delivery to a sample in Bickel is through a prism-slit-Fresnel rhomb focusing lens combination, not "collimating an output from the Raman shifter with a lens, a first dichroic mirror associated with a first beam dump, and a second dichroic mirror associated with a second beam dump" as recited by claim 1. Thus, present independent claim 1, is patentable over the combination of Mandella in view of Alfano, in further view of Bickel.

Further, it is improper to combine Mandella in view of Alfano in further view of Bickel since Bickel provides for "a dispersing prism." Bickel, like Mandella, requires two wavelengths of light. Additionally, Bickel fails to disclose any movement of a sample, but rather delivers the two

wavelengths of light to a sample using a dispersing prism-slit-Fresnel rhomb-focusing lens. Such lens would only further frustrate Alfano, since Alfano requires a focused light of the same wavelength. Thus, a dispersing prism-slit-Fresnel rhomb-focusing lens required by Bickel would frustrate Alfano. Furthermore, Alfano could not produce "fundamental light, harmonic wavelight, and fluorescence" with a dispersing prism slit-Frensnel rhomb-focusing lens. A combination further including Mandella would also not work. A dispersing prism-slit-Fresnel rhomb-focusing lens would operate contrary to the scanner in Mandella that is required to focus two beams of light on a single sample.

Thus, since Bickel would frustrate the purpose of Alfano, Mandella, or any combination thereof, present claim 1 is allowable over the cited combination of Mandella in view of Alfano in further view of Bickel. Claims 12 and 13 depend from claim 1. By virtue of this dependence, claim 12 and 13 are also patentable for at least the same reasons as claim 1.

Claim 23 is also allowable over Mandella in view of Alfano in further view of Bickel for at least the reasons stated above.

The Office Action dated March 12, 2010, in section 7, rejected dependent 9 under 35 U.S.C. § 103(a) as being unpatentable over Mandella in view of Alfano in further view of U.S. Patent Application Publication No. 2003/0013086 to Kask (hereinafter "Kask"). Applicants note that the merits of rejection in section 7 refer to Kask as a paper by Franko.

Claim 9 is canceled by the present amendment and thus, renders moot any rejection thereof.

The Office Action dated March 12, 2010, in section 6, rejected dependent claim 8 under 35 U.S.C. § 103(a) as being unpatentable over Mandella in view of Alfano in further view of Kask. In section 8, dependent claims 16-17 were rejected under 35 U.S.C. §103(a) as being unpatentable over Mandella in view of Alfano and Bickel, and further in view of Kenny (U.S. Patent No. 5,491,344) or Merriam (U.S. Patent No. 6,958,854). Claims 8 and 16-17 are canceled rendering respective rejections moot.

In view of the foregoing, Applicants respectfully submit that all claims presented in this application patentably distinguish over the prior art. Accordingly, Applicants respectfully request favorable consideration and that this application be passed to allowance.

If for any reason the Examiner feels that consultation with Applicants' attorney would be helpful in the advancement of the prosecution, the Examiner is invited to call the telephone number below.

Respectfully submitted,

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Date

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